Class: Rh D Immune Globulin (Human)	Alternate Product Name: • Rh (D) Immune Globulin (Human) • RhIg	Company/Supplier: Saol Therapeutics Research Ltd. (Emergent BioSolutions Canada)

Routes	Intravenous			Other		
	Direct IV	IV Infusion	Continuous Infusion	SC	IM	Other
Acceptable routes*	Yes	Yes	No	Yes*	Yes**	N/A

*Subcutaneous (SC) administration is considered off-label use and may only occur at the direction of the clinical Hematologist for treatment of chronic immune thrombocytopenia (ITP). Intravenous administration is preferred in the setting of ITP treatment, to ensure good absorption.
** Reliable delivery into muscle is necessary to ensure good absorption of RhIg administered for prophylaxis of RhD immunization in Rh negative patients. In obese individuals, the use of a longer (i.e., 1.5") needle into the deltoid muscle is recommended. If intramuscular (IM) delivery cannot be assured, it is highly recommended that intravenous (IV) administration be used instead.

Description	• WinRho® is an Rh Immunoglobulin (RhIg). It is a sterile liquid gamma globulin (IgG) fraction prepared from pooled human plasma containing antibodies to the Rho (D) antigen found on Rh D antigen positive red cells. • Viral reduction steps include filtration, and solvent/detergent treatment. • One 1500 units (300 mcg) vial contains sufficient IgG antibody against the D antigen (anti-D) to effectively suppress the immunizing potential of approximately 15 mL of Rh positive packed red blood cells (or 30 mL of Rh positive whole blood). • **Latex free.**
Availability	• Available in sizes of: 600 units (120 mcg), 1500 units (300 mcg), and 500 units (1000 mcg) single use vials. • Supplied by Canadian Blood Services (CBS). • **Contact your local laboratory/transfusion laboratory service regarding in house stock availability at your site.**
Indications	**1. Prophylaxis of Rh Hemolytic Disease of the Newborn in Pregnancy** • All Rh negative expectant patients at 23-32 weeks gestation (preferred practice is 26-28 weeks) should receive routine antenatal prophylaxis with RhIg, unless they have been confirmed to have formed an immune anti-D. • Routine antenatal prophylaxis with RhIg should be administered regardless of, and in addition to, any RhIg administered for a potentially sensitizing event. • An Rh negative expectant patient who currently demonstrates a passive anti-D (due to prior RhIg injections) may require another RhIg dose, depending on the diagnosis and how much time has elapsed since the initial injection. • All Rh negative expectant patients should receive RhIg within 72 hours of a potentially sensitizing event.

List of sensitizing events for RhD negative peripartum patients necessitating RhIg administration:

Delivery (by any method)	Spontaneous/Therapeutic abortion (medical or surgical)*
Antepartum hemorrhage	Ectopic pregnancy
Chorionic Villus Sampling (CVS)	Abdominal trauma
Amniocentesis	External Cephalic Version (ECV)
Cordocentesis	Intrauterine Fetal Death

* For early loss or termination of pregnancy at less than 8 weeks gestational age confirmed by dating by ultrasound, RhIg administration may be omitted.

- If continued or intermittent bleeding is present, additional doses of RhIg at 3-week intervals may be indicated. Repeat dosing for additional procedures or risks is recommended if 3 or more weeks have elapsed since the last dose.
- All Rh negative post-partum patients of Rh positive or variant D positive babies should ideally receive RhIg within 72 hours of delivery. If more than 72 hours have elapsed, RhIg should be administered as soon as possible, up to 28 days after delivery. Additional dosing will be recommended if the initial fetal-maternal hemorrhage (FMH) screen is positive and Kleihauer-Betke (KB) quantitative testing shows greater than 30 mL of fetal whole-blood in maternal circulation.

2. Incompatible Blood Transfusions

- Rh negative components should be transfused to all Rh negative females of childbearing potential (less than or equal to 50 years of age) whenever possible.
- RhIg should be considered whenever Rh negative females of child bearing potential are exposed to Rh positive donor red blood cells or platelets.
- RhIg should be given to all patients under 18 years of age and patients undergoing allogeneic bone marrow transplantation at any age when Rh Positive platelets are given to an Rh Negative patient.
- It is generally not necessary to administer RhIg to females over 50 years of age or to males 18 years of age or older who receive Rh positive components. However, in certain circumstances (e.g., repeated future transfusions anticipated) it may be considered.

3. Treatment of Immune Thrombocytopenic Purpura (ITP)

- RhIg may be considered as an alternative therapy to intravenous immunoglobulin (IVIg) in a non-splenectomised Rh positive patient **only.**
- RhIg for treatment of ITP **must** be requested by a Hematologist and approved by the Transfusion Medicine Physician on-call.

Contraindications

- In the context of prophylaxis of RhD immunization, RhIg should **NOT** be administered to:
  - Rh positive patients (including babies).
  - Rh negative females of childbearing potential or expectant patients who are RhD sensitized, and confirmed by transfusion medicine laboratory testing to have an allogeneic anti-D.
  - Patients with a history of anaphylactic or other severe systemic reaction to immune globulin concentrates.
  - Patients hypersensitive to product or to any component of its formulation.

	• In the context of ITP treatment, RhIg should **NOT** be administered to:
	  • Rh negative patients.
	  • Splenectomised patients.
	  • Patients with a history of anaphylactic or other severe systemic reaction to immune globulin concentrates.
	  • Patients hypersensitive to product or to any component of its formulation.

Warnings	• WinRho®SDF liquid contains maltose, which can give falsely high blood glucose levels in certain types of blood glucose test systems if given in large doses.
	• Immunoglobulin administration may impair the efficacy of live attenuated virus vaccines (measles, mumps, rubella, and varicella; MMR-V). Vaccination with live virus vaccines should be deferred until approximately 3 months after administration of RhIg, if possible.
	  • The potential risk of lower vaccine efficacy due to possible interference from the RhIg should be balanced against the protection against the vaccine preventable disease.
	  • Patients who have received RhIg after live virus vaccination should undergo serologic testing for antibodies to the vaccine antigens 3 months after vaccination. Women who are found to be non-immune should be revaccinated.
	  • Post-partum patients who have received a live attenuated vaccine in the 14 days prior to receiving RhIg should undergo serologic testing for antibodies to the vaccine antigens 3 months after vaccination. Women who are found to be non-immune should be revaccinated.
	
	• When RhIg is used for the treatment of ITP, a decrease in the patient hemoglobin level may occur since passively administered anti-D attaches to the D antigen on the recipients own red cells. Hemoglobin concentration should be monitored in these patients.
	  • The mean maximum decrease in hemoglobin is this setting is 17 g/L.

Dosage	Dosing of this product is to be determined by the most responsible practitioner (MRP).
	
	1. Prophylaxis of Rh Hemolytic Disease of the Newborn in Pregnancy
	  • If gestational age is known to be less than 12 weeks, a 600 units (120 mcg) dose is sufficient for prophylaxis in the setting of a potentially sensitizing event.
	  • 1500 units (300 mcg) is standard dose for routine antenatal prophylaxis or in the setting of a potentially sensitizing event at or after 12 weeks gestational age.
	  • The routine antenatal prophylaxis dose of RhIg 300 mcg should always be given at 26-28 weeks, regardless of any RhIg doses given in the context of potentially sensitizing events.
	  • For possible sensitizing events at or after 20 weeks gestation **or** following delivery of an Rh positive infant by an Rh negative female, screening for FMH should be ordered by the most responsible practitioner (MRP). A positive result may indicate the need for <u>more</u> RhIg, beyond the standard 300 mcg dose. In the event of a positive quantitative KB test, the Transfusion Medicine Laboratory staff will calculate and communicate a recommended dose to the MRP.

Clinical Scenarios	Gestational Age	WinRho® Dosing
Abortion-medical, surgical or spontaneous; CVS or amniocentesis less than 12 weeks	Less than 12 weeks	120 mcg*†
	12 weeks or more	300 mcg
Threatened abortion **	Less than 12 weeks	120 mcg*†
	12 weeks or more	300 mcg
Routine antenatal prophylaxis at 28 weeks	Approx. 28 weeks	300 mcg
Routine postpartum prophylaxis (If RhD positive neonate) **	At delivery	300 mcg
All other indication ** (e.g., trauma, bleeding in pregnancy)	Less than 12 weeks	120 mcg*†
	12 weeks or more	300 mcg

† May hold WinRho® if there is ultrasound confirmation of gestational age less than 8 weeks gestational age.
*Proceed with 300 mcg if 120 mcg is not stocked.
**FMH testing required at or after 20 weeks' gestation.

2. **Exposure of Rh Negative females of childbearing potential or Rh Negative allogeneic bone marrow transplant patients to Rh Positive donor red blood cells**
   - Recommended dose is between 45 units/mL and 120 units/mL of red cells, depending on route of administration.
   - Consultation with the Transfusion Medicine Physician on-call is required for RhIg dose determination.

3. **Exposure of Rh Negative females of childbearing potential, patients under 18 years old, an Rh Negative allogeneic bone marrow transplant recipients to Rh Positive donor platelets**
   - Recommended dose is 120 mcg following transfusion of 1 adult platelet dose (contains a maximum of 2 mL donor red blood cells within the unit).
   - Consultation with the Transfusion Medicine Physician on-call is required for RhIg dose determination in pediatric patients receiving Rh incompatible platelet transfusion.

4. **Treatment of ITP**
   - Adult recommended initial dose is 125-250 units/kg (25-50 mcg/kg) body weight, depending on the hemoglobin. If the patient has a hemoglobin level of 80-100 g/L, a reduced dose of 125-200 units/kg should be considered to reduce the risk of increasing anemia severity due to hemolysis.
   - Subsequent dosing should be between 125-300 units/kg if required and should be based on the patient's clinical response by assessing platelet counts, and screening for hemolytic complications with hemoglobin and reticulocyte counts, haptoglobin, fractionated bilirubin and dipstick urinalysis.
   - Pediatric ITP recommended dose is 375 units/kg (75mcg/kg) body weight.

Pre-Administration Testing Requirements

- ABO/Rh and antibody screen (Group & Screen) should be performed prior to routine administration of RhIg prophylaxis at 26-28 weeks gestational age and at delivery.
  - The antibody screen of any expectant patient or post-partum patient documented to have received RhIg may have a positive antibody screen for passive anti-D for up to 6 months following administration.
  - Following delivery, cord blood determination of fetal Rh status is required.

	• If the fetus is Rh positive, a Fetomaternal Hemorrhage (FMH) Screen is recommended to determine whether more than a standard RhIg 300 mcg is indicated. • If a historical blood group and a 28-week Group & Screen are available from the current pregnancy and the patient presents with bleeding in pregnancy, a repeat Group & Screen is not required. • In the setting of trauma or bleeding in pregnancy after 20 weeks gestational age, a Kleihauer Betke test is recommended to determine whether a RhIg dose greater than 300 mcg is indicated. • For treatment of ITP or management of Rh Negative females of childbearing potential who have received Rh Positive donor red blood cells in an emergency setting, the following tests are recommended: • Baseline CBC, reticulocyte count, DAT, haptoglobin, fractionated bilirubin, serum creatinine, electrolytes, PTT, INR, fibrinogen and dipstick urinalysis.
Ordering	• Specify dose required. • For ITP treatment, requests or dosage request above the standard dose 600 units (120 mcg) or 1500 units (300 mcg) must be approved by the Transfusion Medicine Physician on-call. • To request product from the transfusion medicine laboratory, use the Blood Product Request Form #103221.
Forms Required	• Informed Consent for Blood Components and/or Plasma Protein Products #101479. • Blood Product Request Form #103221. • Transfusion/Infusion Administration and Assessment Record #101059. • Saskatchewan Transfusion Adverse Event Report Form #103695 (only needed if adverse event occurs). • Notification of Administration of Blood and/or Blood Products Form #103854. • **Forms can be located in the Lab Services Manual. https://www.saskatoonhealthregion.ca/locations_services/Services/Pathology-Laboratory-Med/healthpractitioners/Pages/requisitions.aspx.**
Administration	**Pre-infusion:** • **Blood consent is required** as this product contains a human plasma**.** • Perform all other appropriate pre-administration checks per protocol, detailed in the Nursing Policy and Procedure Blood Components and Plasma Protein Product – Administration of #1141. • Visually inspect the product for particulate matter and discoloration prior to administration **(Do not use solutions that appear cloudy or contain deposits).** • Bring to room temperature. **Administration:** **WinRho® should not be administered concurrently with other products or medications.** **Prophylaxis of Rh Hemolytic Disease of the Newborn in Pregnancy** • IM/IV per most responsible healthcare provider order. • Using a suitable syringe and needle, withdraw the entire contents of the vial to obtain the

labelled dosage of the product.
- Use aseptic technique when preparing and administering WinRho®.

Intravenous (IV) Administration:
- Administer at a rate of injection of 1500 units (300 mcg)/5 to 15 seconds.

  NOTE: If further dilution of WinRho® is preferred prior to intravenous administration, use Normal Saline as diluent. **NO OTHER DILUENT HAS BEEN TESTED.**

Intramuscular Administration:
- Administer the product with the appropriate length needle: 1" for routine, 1.5" for increased BMI patients.
- Administer the product into the deltoid (preferred), ventrogluteal or vastus lateralis muscle, ensuring administration into the muscle. If this cannot be assured, use IV administration.

Exposure of Rh Negative females of childbearing potential to Rh Positive donor red blood cells
- IV administration is recommended due to large doses required.
- Using a suitable syringe and needle, withdraw the entire contents of the vial to obtain the labelled dosage of the product.
- Administer WinRho® 3000 units (600 mcg) IV q8h with a rate of injection of 1500 units (300 mcg)/5 to 15 seconds, until the total recommended dose is given. **NOTE**: If further dilution of WinRho® is preferred prior to intravenous administration, use Normal Saline as diluent. **NO OTHER DILUENT HAS BEEN TESTED.**
- Use aseptic technique when preparing and administering WinRho®.

Exposure of Rh Negative females of childbearing potential, all patients under 18 years of age or Rh Negative allogeneic bone marrow transplant patients to Rh Positive donor platelets
- IM/IV administration per most responsible healthcare provider order.
- Refer to detail above within the **Prophylaxis of Rh Hemolytic Disease of the Newborn in Pregnancy** section.

Treatment of ITP
- IV administration is recommended due to large doses required.
- Using a suitable syringe and needle, withdraw the entire contents of the vial to obtain the labelled dosage of the product.
- Administer the product intravenously with a rate of injection of 1500 units (300 mcg)/5 to 15 seconds. **NOTE**: If further dilution of WinRho® is preferred prior to intravenous administration use Normal Saline as diluent. **NO OTHER DILUENT HAS BEEN TESTED.**
- Use aseptic technique when preparing and administering WinRho®.
- Subcutaneous (SC) administration is considered off-label use and may only occur at the direction of the clinical Hematologist for treatment of chronic immune thrombocytopenia (ITP).

<table>
<tr><td>Nursing Implications</td><td>

- **Patient monitoring:** Follow the Nursing Policy and Procedure Blood Components and Plasma Protein Product - Administration of #1141.
- **Documentation:** Administration and vital signs shall be recorded on the Transfusion/Infusion Administration and Assessment Record #101059.
- Recipients of blood products are to be notified in writing of the transfusion (Notification of Administration of Blood and/or Blood Products Form # 103854).

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<tr><td>Adverse Events</td><td>

- Patients receiving blood product transfusions must be observed closely for signs of any unexpected or untoward reactions.
- Reactions may occur during or after the infusion of blood or blood products, and can range in severity from mild to life threatening.
- Refer to Nursing Policy and Procedure Blood Components and Plasma Protein Product - Administration of #1141 for managing of allergic transfusion reaction and call MRP.
- Document adverse event on Saskatchewan Transfusion Adverse Event Report Form #103695, whether or not the transfusion was discontinued

- **Adverse reactions with RhIg administration (usual dose) by any route:**
  - Common - Pain or discomfort at the injection site, headache
  - Uncommon - chills, fever, nausea/vomiting, hypotension, arthralgia, moderate low back pain, rash.

<table>
<tr><td>Adverse Reactions - Minor
- Flushing
- Headache
- Itching and redness at the venipuncture site</td><td>Action

Slow rate of administration</td></tr>
<tr><td>Adverse Reactions – Major
- Hives/Severe itching
- Cough
- Chest pain
- Wheezing
- Facial swelling
- Feeling lightheaded/dizzy or fainting</td><td>Actions

STOP Infusion
IMMEDIATELY and contact most responsible healthcare provider</td></tr>
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Intravenous administration of RhIg in large doses for ITP (Rh Positive patients) or following exposure of Rh Negative females of childbearing potential to Rh Positive donor red blood cells:

- Following administration patients should be closely monitored using clinical and laboratory parameters for at least 8 hours after the final dose of RhIg for potential adverse reactions including signs and/or symptoms of intravascular red blood cell hemolysis.
  - Clinical signs and symptoms of hemolysis include pallor, hypotension, tachycardia, hemoglobinuria (red urine).
    - Severe clinical complications of hemolysis include renal failure (oliguria or anuria and edema), and coagulopathy (increased bruising or bleeding).
  - A dipstick urinalysis should be performed at baseline and then after administration at 2

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	hours, 4 hours and prior to the end of the monitoring period.
	• If signs and/or symptoms of hemolysis are present or suspected after RhIg administration, the following laboratory tests should be performed:
	  • CBC, haptoglobin, DAT, fractionated bilirubin
	  • Serum creatinine, electrolytes
	  • INR, PTT, fibrinogen
	  • Urinalysis
	• The Transfusion Medicine Physician on-call should be notified in the event of any suspected cases of intravascular hemolysis associated with RhIg administration.
	• Prior to discharge, patients should be instructed to self-monitor for signs and symptoms of intravascular red blood cell hemolysis for least 72 hours, these include symptoms of back pain, discoloration of urine, hematuria, shaking chills and fever and should be advised to seek medical attention **immediately.** (Absence of signs and/or symptoms of hemolysis within 8 hours does not guarantee that it cannot occur subsequently).

Storage and Stability	• Stored at 2-8^{o}C. **Do not freeze.** • Expiration date is indicated on bottle and packaging.
Comments	• WinRho® SDF Product Monograph, Date of Approval March 31, 2020. Submission Control #: 211513. https://winrho.com/canada.php Accessed November 17, 2022. • WinRho® FAQs https://saskblood.ca/prams-program/ , WinRho FAQs December 2022 Version. • Blood products, human immunoglobulin and timing of immunization: Canadian Immunization Guide. https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-1-key-immunization-information/page-11-blood-products-human-immune-globulin-timing-immunization.html Accessed September 9, 2022. • American College of Obstetricians and Gynecologists. Practice bulletin no. 181: prevention of Rh D alloimmunization. Obstetrics & Gynecology. 2017 Aug:130(2):e57-e70.